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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR		ATTORNEY DOCKET NO.
08/955,572	10/22/97	KWON	B	IND4-DI1B

HM12/0117
SCHWEGMAN, LUNDBERG, WOSSNER & KLUTH, P.A.
P.O. BOX 2938
MINNEAPOLIS MN 55402

EXAMINER	
LANDSMAN, R	
ART UNIT	**PAPER NUMBER**
1647	35

DATE MAILED: 01/17/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	08/955,572	KWON, BYOUNG S.	
	Examiner	Art Unit	
	Robert Landsman	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5,6,24 and 26-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5,6,24 and 26-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

1. Formal Matters

A. Amendment I, filed 10/31/00, has been entered into the record.

B. The Raw Sequence Listing, filed 2/28/00, has been entered into the record.

C. Claims 5, 6, 24 and 26-31 are currently pending in the application.

D. All 35 USC Statues not found in this Office Action can be found, cited in full, in a previous Office Action.

Maintained Objections

1. Oath/Declaration

A. Applicants have stated that they will submit a substitute Declaration to obviate the Examiner's objection on page 2 of the Office Action dated 4/27/00. However, at the time of this Office Action, no Declaration has been filed. Therefore, the objection stands.

Maintained Rejections

A. Claims 5, 24 and 26-31 remain rejected under 102(a) as being unpatentable over Alderson et al. for the reasons already of record on page 9 of the **Office Action dated 8/24/99**. The rejection was initially withdrawn in the Office Action dated 4/27/00 since Applicants' argued that the present application is a DIV of 08/122,976, filed on 9/16/93. However, the present application does not claim priority to this application in the Declaration, or in the first line of the specification. Therefore, this rejection has been reinstated until Applicants claim priority to 08/122,796 in the specification.

Withdrawn Rejections

1. Claim Rejections - 35 USC § 112, first paragraph

A. The rejection of claim 26 under 35 USC 112, first paragraph, regarding the use of a composition, has been withdrawn since Applicant amended the claim to remove the word "pharmaceutical."

B. The rejection of claims 5 and 26-31 under 35 USC 112, first paragraph regarding these claims reading on a gene has been withdrawn since the claimed protein comprises an entire open reading frame.

2. Claim Rejections - 35 USC § 112, second paragraph

A. The rejection of claims 28 and 30 under 35 USC 112, second paragraph, regarding "specifically hybridizes" have been withdrawn since Applicants have amended the claims to remove this phrase.

New Objections

A. Claim 6 is objected to. It is suggested that the phrase "shown in" be replaced with "of."

New Rejections

1. Claim Rejections - 35 USC § 112, first paragraph - scope

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A. Claims 5, 24, 26, 27, 29 and 31 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO:2, does not reasonably provide enablement for a

"**fragment**" of SEQ ID NO:2 or of an extracellular domain of SEQ ID NO:2. Nor does it provide enablement for a fragment of "**residues 1-186**" of SEQ ID NO:2, or for a protein encoded for by a "**combination**" of SEQ ID NOs. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

First, the breadth of claim 1 is extensive with regard to claiming all "**fragments**" of SEQ ID NO:2 and a fragment of "**residues 1-186**" of SEQ ID NO:2. Furthermore, Applicants provide no guidance or working examples of these fragments, nor do they provide a *function* of these "fragments", or how these fragments of SEQ ID NO:2, or of the extracellular domain of SEQ ID NO:2, will retain activity. They also do not demonstrate what the function of a protein encoded for by a "**combination**" of SEQ ID NOs is. A protein comprised of a combination (i.e. 2 or more) SEQ ID NOs. would be expected to have a different tertiary structure as well as different ligand binding and functional capabilities compared to a protein comprising only one SEQ ID NO.

Regarding "fragments" of the claimed proteins, it has not been shown that these fragments contain a binding domain of the protein which interacts with (e.g. binds) H4-1BB ligands. Furthermore, it is not predictable to one of ordinary skill in the art what the functions of these fragments are, including those which do not comprise a ligand binding domain. Nor is there any guidance or working examples of what the function of a protein comprising a combinantion of SEQ ID NOs is, nor is it predictable to one

of ordinary skill in the art what the function of a protein comprising a combination of SEQ ID NOs. qould be.

In summary, the breadth of the claims is extensive with regard to Applicants claiming all fragments of SEQ ID NO:2. There is also a lack of guidance and working examples of functional fragments, as well as which of these fragments are able to retain activity, nor what that activity is. These factors, along with the lack of predictability to one of ordinary skill in the art as to what the functions of these fragments of SEQ ID NO:2 are, or of a protein comprising a combination of SEQ ID NOs, leads the Examiner to hold that undue experimentation is necessary to practice the invention as claimed.

2. Claim Rejections - 35 USC § 112, first paragraph – lack of written description

A. Claims 5, 24, 26, 27, 29 and 31 are genus claims. The term "**fragment**" means a protein having one or more amino acid deletions to either or both the NH2 terminus and the COOH terminus of SEQ ID NO:2. The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. The specification and claims do not place any limit on the number of amino acid deletions that can be made to SEQ ID NO:2. Thus the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Although these types of changes are routinely done in the art, the specification and claims do not provide any guidance as to what changes should be made.

Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO:2 alone are insufficient to describe the genus. One of skill in the art would reasonable conclude that the

disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus at the time the invention was made.

Similarly, the specification provides a written description of a single species of protein, SEQ ID NO:2. No other species of protein is described, or structurally contemplated, within the instant specification. Therefore, one skilled in the art also cannot reasonably visualize or predict what critical amino acid residues would be necessary to maintain the functional characteristics of a fragment of SEQ ID NO:2 consisting or comprising only of **residues 1-186**, or of a protein comprising a **combination** of SEQ ID NOs. because it is unknown and not described what constitutes a functional protein consisting or comprising less than, or more than, the full-length open reading frame of SEQ ID NO:2. Therefore, the written description requirement under 35 USC 112, first paragraph, has not been met.

3. Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 5 recites the limitation "The protein" in the preamble. There is insufficient antecedent basis for this limitation in the claim. Appropriate correction is required. It is suggested that the claim be amended to recite "A protein..."

B. Claims 5, 24, 26-31 are confusing since it recites the term "soluble." All proteins, or fragments of proteins, are soluble in the appropriate solvent. The type of solvent should be specified, e.g. "water-soluble."

C. Claims 5 and 27 are confusing since the claims refer to both a "protein" and a "fragment." It is not clear, in claim 5 for example, whether the "protein" of the preamble and the "protein" being purified as recited in part (c) of the claim includes the "fragment." It is suggested that the term "protein" be amended to recite a "polypeptide" to encompass both "proteins" and "fragments."

D. Claim 27 is confusing since it is not clear whether the *extracellular domain* of H4-1BB has SEQ ID NO:2 or if the extracellular domain is *contained* in the full-length protein of SEQ ID NO:2.

E. Claims 28 and 30 are confusing because of the term "combination." It is not understood how the protein of the claim can comprise more than one nucleic acid sequence.

4. Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

A. Claims 5, 24, 26 are rejected under 35 U.S.C. 102(b) as being anticipated by the Sigma Chemical Company (1992). These claims are directed to a fragment of SEQ ID NO:2, or of the extracellular domain thereof as well as a composition comprising a fragment. The Sigma catalogue teaches a fragment of SEQ ID NO:2 comprising Leu (page 1419, Product No. L1512) as well as Leu in solution (page 1405, Product No. L0389). Since a fragment of SEQ ID NO:2 of the claim can be only one amino acid, the Leu taught by the Sigma catalogue meets the limitation of the claims.

5. Claim Rejections - 35 USC § 101 – provisional obvious-type double patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 5, 6, 24 and 26-31 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 19, 22, 23, 29, 31, 32, 33, 34 and 36 of copending Application No. 08/948,764. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons:

A. Claims 5 and 6 of the instant application recites a protein of SEQ ID NO:2, or a soluble fragment of SEQ ID NO:2 Claims 24, 27, 28 and 30 recite that this fragment is an extracellular domain of SEQ ID NO:2 encoded by SEQ ID NO:1. Claim 26 recites a composition comprising the extracellular domain of the protein of claim 24. Claims 29 and 31 recite that the protein fragment comprises amino acids 1-186 of SEQ ID NO:2. Claims 22, 23, 31, 33 and 36 of the co-pending Application No. 08/948,764 recite a protein of SEQ ID NO:2 comprising an extracellular domain encoded for by SEQ ID NO:1 wherein the protein or fragment can bind a cell membrane ligand.

The difference between the instant application and the co-pending application is that claim 5 of the instant application does not require the fragments of SEQ ID NO:2 to be from the extracellular domain, nor does it require that SEQ ID NO:2 be encoded for by SEQ ID NO:1, nor that the protein or fragment bind ligand. In addition, the co-pending application does not recite amino acids 1-186 of SEQ

ID NO:2. However, it would be obvious to one of ordinary skill in the art that the fragments of claim 5 could comprise the extracellular domain of SEQ ID NO:2 and that, regardless of the nucleic acid molecule which encodes the protein, SEQ ID NO:2 is the same protein in both applications and that a protein (claims 5 or 6), or an extracellular domain (claim 24), from the instant application would be the same protein or extracellular domain from the co-pending application and would, therefore, be expected to bind the same ligands. It would also be obvious, therefore, that the compositions comprising an extracellular domain of the instant application would be obvious over that of the co-pending application. Furthermore, amino acid residues 1-186 of SEQ ID NO:2, as recited in claims 29 and 31 of the instant application, do comprise the extracellular domain of SEQ ID NO:2 as taught in the co-pending application.

In summary, the claims of the instant application are broader than, and encompass those of the co-pending application. Similarly, the fragments of the instant application would be obvious over the fragments claimed in the co-pending application since, though the fragments of the instant invention do not recite the limitation that they need to, for example, comprise the extracellular domain of human 4-1BB and bind a cell membrane ligand, one would be motivated to make the fragments of the instant invention to use them, for example, as antigen for antibody production.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
January 16, 2001

Gary L. Kunz

GARY L. KUNZ
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600